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I, Andrew Wilford, a citizen of the United States of America, residing in Dobbs Ferry, New York, depose and state that:

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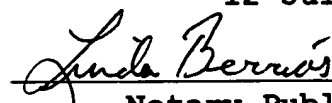
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Andrew Wilford

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12 July 2006

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METHOD OF ENRICHING HYPERPOLARIZED ATOMIC NUCLEI

AND AN APPARATUS FOR IMPLEMENTING THE METHOD

The invention relates to a method of enriching
hyperpolarized atomic nuclei and an apparatus for carrying out the
method.

Recent developments in magnetic resonance tomography
(MRT) and magnetic resonance spectroscopy (NMR) with polarized
noble gases anticipate applications in medicine, physics and
materials science. Large polarizations of nuclear spins of noble
gases may be achieved by optical pumping using alkali atoms, as
described in the publication Happer, et al., Phys. Rev. A, 29,
3092 (1984).

Through optical pumping by incident light radiation into
matter, the occupation numbers of certain energy states are
increased significantly relative to the state of equilibrium.
Polarization thereby refers to the degree of orientation (ordering)
of the spins of atomic nuclei, or electrons. For instance, 100
percent polarization means that all nuclei or electrons are
oriented likewise. Polarization of nuclei or electrons is tied to
a magnetic moment.

Hyperpolarized ^{129}Xe is, for instance, inhaled by or
injected into a human being. The polarized xenon accumulates 10 to
15 seconds later in the brain. The distribution of the noble gas
in the brain is determined by using magnetic resonance tomography.
The result is used for further analysis.

Choosing a polarized noble gas depends in each case on its actual application, ^{129}Xe has a great chemical shift. If, for example, xenon is adsorbed on a surface, its resonance frequency changes significantly. Moreover, xenon is soluble in lipophilic

5   liquids. When such properties is desired, xenon is used. The noble gas helium is hardly soluble in liquids. The isotope ^{3}He is therefore regularly used, when cavities are concerned. The human lung is an example of such a cavity.

Some noble gases exhibit other useful properties. The

10   isotopes ^{83}Kr, ^{21}Ne and ^{131}Xe have a quadruple moment that is of interest, e.g., for experiments in basic research or surface physics. However, these noble gases are very expensive, which makes them unsuitable for applications, in which greater amounts are used.

15   From the publication Driehuys et al. (Appl. Phys. Lett. (1996). 69, 1668) it is known how to polarize ^{129}Xe in a polarizer in the following way.

Based on a gas supply, a gas flow consisting of a mixture of 1 % ^{129}Xe and N$_2$, including 98 % ^{4}He, is mixed with Rb vapor in a

20   container and conducted through a test cell. Using a laser, circular polarized light is produced, i.e. light in which the spin momentum or the spin of the photons has the same direction. In the test cell, the Rb atoms are optically pumped as an optically pumpable species by the laser beam ($\lambda \sim$ 795 nm, Rb Dl line)

25   longitudinally to a magnetic field, thereby polarizing the electron spins of the Rb atoms. The spin momentum of the photons is thereby transferred to the free electrons of the alkali atoms. The spins

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of the electrons of the alkali atoms vary greatly from thermal

equilibrium, i.e. the alkali atoms are polarized. Through the

collision of an alkali atom with a noble gas atom, the polarization

of the electron spins is transferred from the alkali atom to the

5   noble gas atom, whereby polarized noble gas forms. The

polarization of the electron spin of the alkali atoms created by

optical pumping of alkali atoms is thus transferred through spin

exchange of the alkali electron to the nuclear spin of the noble

gases.

10   Alkali atoms are used, since they possess a large optical

moment of dipole, which interacts with light. Furthermore, alkali

atoms exhibit a free electron, so that unfavorable interactions

between two or more electrons per atom cannot occur.

The partial pressure of ^{4}He in the gas mixture is up to

15   10 bar. Compared with other partial pressures (xenon or nitrogen),

this is very high. This relatively high partial pressure means

that polarized atoms only rarely reach the test wall of the glass

cell and lose their polarization there, e.g., through interaction

with paramagnetic centers. With an increasing partial pressure of

20   ^{4}He, the probability of the polarized atoms hitting the cell wall

decreases.

The heavy noble gas atoms, e.g. xenon atoms, give rise to

strong relaxation of the polarization of the optically pumped

alkali atoms when colliding with the alkali atoms. In order to

25   retain maximum polarization of the alkali atoms during optical

pumping, the partial pressure of the xenon gas in the gas mixture

must be correspondingly low. Even with a partial pressure in the

gas mixture of 0.1 bar, a laser capacity of around 100 Watt is required in order to achieve a polarization of the alkali atoms of about 70 percent in the whole test volume.

For ^{129}Xe, the nuclear-spin polarization formation times are between 20 and 40 seconds due to the high spin exchange of the cross section. Due to the very high rubidium-spin destruction rate for rubidium xenon collisions, the xenon partial pressure may not exceed stated values, so that a sufficiently high rubidium polarization may be maintained during optical spin-exchange pumping. Hence ^{4}He is employed as a buffer gas in such polarizers to achieve line broadening.

Test cells of glass are employed, blown from one piece, and in which the noble gas atoms or the atomic nuclei are optically pumped.

According to the prior art, the test cell is placed in a static magnetic field B0 of about 10 Gauss produced by coils, especially a pair of so-called Helmholtz coils. The direction of the magnetic field extends parallel to the cylinder axis of the test cell, or parallel to the direction of the laser beam. The magnetic field serves to guide the polarized atoms. The rubidium atoms, which are optically highly polarized due to the laser light, collide in the glass cell, e.g. with the xenon atoms, and release their polarization to the xenon atoms.

Typical values of partial pressure at the exit of a polarizer are p_{He} ~ 7 bar, p_{N2} ~ 0.07 bar, p_{Xe} ~ 0.07 bar at a numerical particle density of Rb of ~ 10^{14} cm^{-3}. With hyperpolarization of ^{129}Xe, its partial pressure is limited during

polarization to about 0.1 bar due to spin-exchange optical pumping. In order to produce a sufficient and satisfactory amount and thickness of hyperpolarized gas for many applications, Xe thickness in the gas needs to be increased for enrichment.

5   A method of enriching hyperpolarized ^{129}Xe is disclosed in European Patent EP 0 890 066 Bl. During the process, a gas mixture containing hyperpolarized ^{129}Xe flows through an enrichment reservoir. The reservoir is cooled, e.g. with liquid N_2 to a temperature at which xenon condenses to a frozen state, whereby it

10   is enriched in frozen state in the reservoir from the flowing output gas. Rubidium settles on the wall at the exit of the test cell due to the high melting point compared with the melting points of the other gases. The polarized ^{129}Xe or the residual gas mixture is carried further by the test cell into a freezing unit, which

15   consists of a glass flask, whose end is submerged in liquid nitrogen. The glass flask is situated in a magnetic field with a strength up to 1 Tesla. To obtain long enrichment times of ^{129}Xe of about 1 hour, a magnetic field must be applied on a magnitude of about 1 T, since with weaker magnetic fields and a temperature of

20   liquid N_2, the relaxation time of the polarized Xe ice is only a few minutes, so that considerable parts of the polarization again decay for long enrichment times. Longer relaxation times (Tl ~ a few hours) can only be obtained, when the Xe ice is enriched/stored at a temperature of the liquid He of about 4 °K.

25   Disadvantageously, the ^{129}Xe thus needs to be frozen very quickly and preferably without any loss, following polarization, by using a strong magnetic field of about 1 T, stored and subsequently

re-vaporized in Xe gas. Only about 1 to 2 hours remain for using
the noble gas, before the xenon polarization through relaxation has
declined to such an extent that further use is no longer possible.
The complexity of preparing strong magnetic fields and temperatures
in order to condense ^{129}Xe makes this process expensive and
cumbersome.

The object of the invention is to provide a method for
enriching hyperpolarized atomic nuclei at a reasonable cost.
A further object of the invention is to make available an apparatus
for carrying out the method.

This object is attained by a method with the totality of
the features of claim 1, and by an apparatus as claimed by the
dependent claims. Advantageous embodiments follow from the related
claims.

The process provides for the solution of hyperpolarized
atomic nuclei, flowing in a gas mixture, in a solvent cooled to
below 293 K.

Solubility is defined as the density of the
hyperpolarized gas in the solvent relative to the density of the
hyperpolarized gas in the gas chamber situated above a given
temperature and pressure. The solubility is also referred to as
the Ostwald coefficient.

Within the scope of the invention, it was recognized that
by using a solvent cooled below room temperature, especially an
organic solvent, such as a hydrocarbon, it was possible to obtain a
large increase in gas density in the solvent compared to the gas
phase. In the solvent cooled below room temperature, a solubility

of at least twice that at room temperature is obtained, which is used for the hyperpolarized atomic nuclei in the solvent.

The solvent below room temperature has an Ostwald coefficient of at least 2 for the hyperpolarized atomic nuclei.

5   With decreasing temperatures, solubility or the Ostwald coefficient increases to values of up to 200. Above room temperature, the Ostwald coefficient may advantageously assume a value below 1.

The method according to the invention is by no means limited to enrichment of hyperpolarized atomic nuclei. Rather, it

10 was found that the process will always be useful when a certain component to be enriched in a gas mixture is especially easily soluble in comparison with other components of the mixture in a solvent cooled below 93 °K.

For example, the enrichment of carbon isotopes ^{12}C and ^{13}C

15 from a mixture of N_2 and 02 may be mentioned. Following solution in a solvent cooled below room temperature, the carbon isotopes are enriched and separated from N_2 and 0_2. Subsequently ^{12}C and ^{13}C are separated through isotopic separation. Any valuable gas from a mixture may be enriched and possibly separated through further

20 steps of the method. The method has the advantage of being economical and easy to handle.

In a further embodiment of the invention, a lipophilic solvent with high viscosity is chosen for the method.

As solvent for hyperpolarized ^{129}Xe, toluol with a Ostwald

25 coefficient of about 5 is, for example, chosen as the standard conditions (293 °K, 1 bar), or ethanol with an Ostwald coefficient of about 2.5 at standard conditions.

Pentane, acetone/methanol and butanol are generally suitable solvents for enrichment of hyperpolarized noble gases. The solvent may be chosen according to the temperature.

In an especially advantageous embodiment of the invention, the solvent is present in liquid phase even at low temperatures, e.g. 180 °K.

In a further embodiment of the invention, the melting point of the solvent decreases compared with the pure solvent without the hyperpolarized atomic nuclei.

Such a decrease of the melting point was determined within the scope of the invention in the case of toluol, in which ^{129}Xe was dissolved.

Dissolving hyperpolarized atomic nuclei in the solvent is thus done at temperatures that are lower than expected from prior art. This effect is used for enrichment, since lower temperatures result in a rapid increase of solubility.

As solvents, olive oil and benzol also exhibit a high Ostwald coefficient.

A suitable choice of solvent will ensure the desired increase of solubility and thus enrichment of the hyperpolarized atomic nuclei in the solvent.

The solvent comprises, for example, ethanol and/or toluol. For both solvents within the scope of the invention, a large solubility below room temperature was determined for hyperpolarized atomic nuclei. It is conceivable that these solvents may be used for enrichment of other components from a gas mixture, such as ^{13}C.

In the case of hyperpolarized atomic nuclei to be
enriched, their Ti relaxation times in the solvent during the
process is chosen greater than their residence time in the solvent.
Deuterized solvents, such as $C_6D_5CD_3$ (toluol) or CD_3CD_2OD (ethanol),
in which the relaxation times of the hyperpolarized atomic nuclei
are greater than 100 seconds, may be chosen.

Dissolving a hyperpolarized noble gas in a solvent from
the gas flow of a polarizer is preferably done in a chamber, in
which the solvent is either present in cooled condition or is still
undergoing cooling. Similarly, other gases to be enriched are
conducted into such a chamber.

The process optionally provides for introducing degassing
from the solvent after dissolving a component to be enriched, e.g.
a hyperpolarized noble gas. For this purpose, the solvent may be
conducted out of the cooling chamber into a further chamber for
degassing.

Solution and degassing may conceivably be performed in
one and the same chamber, provided the chamber has cooling and
heating means.

The volume of the chambers, especially the chamber in
which degassing occurs, is chosen sufficiently large, so that if
hyperpolarized atomic nuclei are being enriched, the relaxation
times of the nuclei through wall contact is longer at the inner
walls than is the enrichment times.

The T_1 time of hyperpolarized atomic nuclei is
determined, e.g. by their interaction with the inner wall of the
chamber. By coating the inner walls of the chambers and/or the

connection lines between the chambers, e.g. with deuterized

monochlorosilane or PFA (perfluoroalkoxy compounds), T_1 times

exceeding one hour may be obtained. For instance, for Xe gas, a

fundamental T_1 (Xe-Xe interaction) time of 56 h/p (amagat) may be

5   applied.

With the method according to the invention hyperpolarized

atomic nuclei may therefore be enriched and stored for a longer

period than with the known methods.

During the enrichment process, multiple repetition of the

10   solution and degassing steps of the components to be enriched or

the hyperpolarized atomic nuclei in and from a cooled solvent may

be done in an especially advantageous manner. Especially, the

solvent may be conducted in chambers especially provided for this

purpose. This procedure may bring about a pump effect and for

15   enrichment, an increased density of the components to be enriched.

The flow of the solvent may be controlled continuously or

semi-continuously via the pressure in the chambers or in the

pressure compensation containers or tanks.

In the case of hyperpolarized [129]Xe as a component to be

20   enriched, the process has the advantage that depending on the

solvent only minor amounts of N_2 are dissolved in the storage

medium, whereas with known freezing methods, considerable amounts

of N_2 are frozen.

An apparatus for carrying out the method therefore

25   comprises at least one chamber with means for degassing the

enriched components dissolved in a solvent situated in the chamber.

For the purpose of degassing, the chamber is provided with, e.g.
heating coils and/or means for producing ultrasound.

For a hyperpolarized noble gas as a component to be
enriched, the apparatus features at least one means for forming a
magnetic field with a strength not exceeding 0.04 Tesla, e.g. a
Helmholtz coil.

As an advantage, expensive and heavy magnets for
generating magnetic fields for the hyperpolarized atomic nuclei are
thus no longer needed.

Instead, simple Helmholtz electromagnets, or permanent
magnets suffice, since the cooled solvent must be exposed to a
maximum magnetic field of only 0.04 Tesla for enrichment. This
affects the mobility afforded by such apparatuses.

When solution and degassing occur in the same chamber,
the chamber features means for degassing, and possibly cooling.

The method according to the invention enables enrichment
of hyperpolarized atomic nuclei at a considerably higher
temperature than is used according to prior art. The temperature
of the solvent may be set to, e.g. about 180 °K during enrichment,
versus 77 °K if condensed Xe-Sis is used. The temperature needed
for the enrichment method using solvents according to the invention
may thus be obtained through standard cooling methods or coolants,
e.g. Peltier elements. This advantageously allows for a compact
design of the apparatus according to the invention for mobile
systems.

If degassing is done in another chamber, the apparatus
features at least one chamber, in which the hyperpolarized atomic

nuclei or other components to be enriched are dissolved, and a
further, second chamber connected with this chamber. The cool
solvent containing the gas to be enriched is conducted from the
first to the second chamber, where degassing is done. The second
5   chamber thereby has the said means for degassing from the solvent.

The apparatus may have a tank for the enriched gas, such
as a hyperpolarized noble gas. This tank is connected with the
chamber(s) in which degassing is done. The enriched, possibly
hyperpolarized gas is introduced into the tank, whereas the solvent
10   is disposed of, or returned under cooling to the cooling chamber.
In an especially advantageous embodiment of the invention, the
apparatus has at least two units connected successively, each
consisting of a chamber, in which the component to be enriched,
e.g. a hyperpolarized noble gas is dissolved in a cooled solvent,
15   and a further chamber, in which the solvent is degassed a second
time. The solution and degassing process may thus be repeated and
carried out in two stages, for example. This advantageously
results in a further increase in solubility or enrichment in the
solvent.

20   The solvent cooled beneath 293 °K may, of course, be used
not only for enrichment, but also for storing and transporting a
component, e.g. a certain hyperpolarized noble gas, to be enriched.
Once enriched, gases, especially hyperpolarized noble gases, are
however also of special interest in the cooled solvent, as the
25   method according to the invention is not limited to the above-
mentioned advantages. In many applications, it is necessary to
make available, e.g. hyperpolarized ^{129}Xe pre-dissolved in a liquid

in order to carry it to the objects or substances to be examined, e.g. complex molecules, or examine the diffusion of liquids in porous structures. The step involving thawing from the Xe ice is advantageously omitted in the method according to the invention.

5   A cooled solvent containing a dissolved hyperpolarized noble gas is therefore a direct contrast agent for magnetic resonance tomographic examinations.

Cooled ethanol or toluol with dissolved ^{129}Xe may be also mentioned as an example.

10   A cool solvent containing hyperpolarized atomic nuclei, or ^{13}C, 235U or 238U, whereby the solvent has a temperature of below 293 K, is therefore of special interest. The solvent may, besides toluol or ethanol, also comprise pentane or other solvents. Such a solvent may

15   The invention is explained in more detail in the following with reference to the examples and attached figures.

FIG. 1 shows measuring results for the solubility of ^{129}Xe in toluol and ethanol depending on the temperature of the solvent.

FIG. 2 shows an apparatus for carrying out the method

20   according to the invention.

According to FIG. 1 it appeared surprisingly that already at a temperature of 273 °K, a clear increase of the solubility or Ostwald coefficient of ^{129}Xe is obtained compared to at room temperature.

25   At a temperature of about 240 °K, a ten times higher density of ^{129}Xe compared with the gas phase is already obtained both in ethanol and toluol. An even higher solubility of ^{129}Xe in

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the solvent is obtained by cooling to temperatures of 180 °K, thereby obtaining a 100-fold increase of the density in both toluol and ethanol compared to the gas phase. Further cooling by just a few degrees Kelvin already results in an increase of the Ostwald

5   coefficient to a value of 200 (FIG. 2).

A further sharp rise of solubility occurs, when the solvent is further cooled. This effect may also be produced with other solvents and hyperpolarized atomic nuclei, or with ^{13}C, low temperatures is especially interesting, since with a solution of

10 hyperpolarized atomic nuclei, a reduction of the melting point of the solvent relative to pure solvent without hyperpolarized atomic nuclei can be detected, and is also expected for other solvents.

A typical enrichment apparatus is shown in FIG. 2. A gas mixture 1 with hyperpolarized atomic nuclei flows from a

15 polarizer (not shown) into a first chamber 2 containing a cooled solvent. Chamber 2 has means for cooling the solvent. The solvent containing the gas mixture is thereby cooled to a temperature T_1 of, e.g. 180 °K.

The gas components are enriched in chamber 2 according to

20 their solubility in the solvent, and thus separated from one another. The unnecessary components of the mixture are released through valve 3. The solvent enriched with the hyperpolarized atomic nuclei is guided through a connection line out of chamber 2 into a further chamber 5. Chamber 5 comprises means for degassing,

25 such as an apparatus for producing ultrasound and/or heating. Degassing of the solvent therefore occurs as a result of heat and/or ultrasound in chamber 5.

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Chamber 5 thus represents a degassing chamber 5 for the hyperpolarized atomic nuclei from the solvent. In chamber 5, a gas pressure of the originally dissolved gas arises due to the degassing of the hyperpolarized atomic nuclei via the solvent. The gas pressure is determined by the partial pressure of the hyperpolarized atomic nuclei (gas component) in solvent chamber 2, and the ratio of the solubilities of this gas component in the solvent at temperatures T_1 in chamber 2 and T_2 in chamber 5.

The volume of degassing chamber 5, into which the solvent is guided, is sufficiently large in order to ensure a long T_1 relaxation time of the hyperpolarized nuclei. The volume is dimensioned such that a gas pressure of about 2 bar is set. Following degassing in chamber 5, the solution and degassing process may be repeated, as represented in FIG. 2 by continuous lines. For this, starting from chamber 5 at the end of the first enrichment stage, the gas with the hyperpolarized atomic nuclei is guided into chamber 6, where it is cooled to the temperature T_1. Following enrichment in the solvent, the gas is conducted into chamber 8 with a temperature of T_2 for degassing. Chamber 8, again, has a sufficient volume.

Chamber 6 is provided with a cooling unit 7 for cooling the solvent, as is chamber 2.

The respective temperatures T_1 and T_2 in chambers 2, 6, as well as 5, 8, may but need not be identical. Instead, the chambers may be provided with heating apparatuses and means for producing ultrasound, depending on the actual application. The degassed

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hyperpolarized atomic nuclei are guided from chamber B into a tank 9.

The inner walls of the tank 9 are lined with PFA or monochlorosilane in order to prolong the relaxation time of the hyperpolarized atomic nuclei. Basically, all chambers and

5   connecting lines of the apparatus may be designed like this. The solvent is fed into a waste container 14 and disposed of, or stored temporarily for reuse in a container 10. The transport may be controlled by the gas pressure by exposing the solvent to pressure compensation, e.g. in container 10. The waste container

10   14 is arranged behind either chambers 5 or 8 for degassing. Subsequently, the solvent is returned through a cooling coil via connecting line 12 to chamber 2.

A storage tank 13 containing solvent is arranged before the cooling coil 11, so that spent solvent is replaced and may be

15   pre-cooled to the intended temperature T_1.

The complete process may be controlled continuously or semi-continuously via the pressure tank 9 and pressure compensation container 10.

The process may be controlled at least partially via the

20   drawn valves. Additional valves not shown may be arranged, e.g. behind chamber 8 before the branching off after waste container 14. The process may also be performed in one step, as indicated in FIG. 2 by the dotted lines. Then, valves that are not shown ensure that the solvent released from chamber 5 may be fed into the pressure

25   compensation container 10, or else an equivalent three-way valve may be inserted before the pressure compensation container.

To store the gas in tank 9, a magnet field below 0.01 T need only be provided, whereby Helmholt coils are appropriately arranged as a part of the apparatus.

The following ^{129}Xe densities in the solvent (toluol/ethanol) may be set at different temperatures:

	Stage 1	Stage 2
	(Chamber 2)	(Chamber 6)
T = 240 °K,	pXe,Sol -0.7 bar	~3.5 bar
T = 200 °K,	pXe,Sol -2.1 bar	~10 bar
T = 180 °K,	pXe,Sol -7.0 bar	~20 bar

Similar values are obtained for pentane, acetone, methanol and other solvents.

Naturally, another valuable gas may be enriched, e.g. ^{13}C, using such an apparatus.